

Applicants respectfully direct the Examiner to the specification at page 20, lines 5-10, which teaches that the group of proteins having PDZ domains "... share a common property of interacting with other proteins having the region of hydrophobic amino acids on the C-terminus. These and other proteins can be isolated by the screening methods of the present invention." Applicants submit that this description clearly describes that the proteins of the invention can be used to isolate various proteins that have hydrophobic amino acid regions at the C-terminus. In support of this position, Applicants provide the attached declaration of Dr. Shin-Ichi Funahashi under 37 C.F.R. §1.132.

Dr. Shin-Ichi Funahashi utilized techniques taught in the specification at, for example, page 23 to 24, as well as techniques known in the art, in combination with the novel polypeptides of the invention to identify proteins having hydrophobic amino acid regions at the C-terminus. The data submitted by the §1.132 Declaration show that among the proteins provided by Applicants' specification comprising PDZ domain, fragments of SEQ ID Nos: 1 and 2 containing the so-called I-K domains and L-M domains can be used to screen for various useful proteins including proteins having a hydrophobic amino acid region at the C-terminus. For example, known proteins such as OBTP, Galectin-3, Muc12, and BAI3 were isolated in this screen by their ability to bind to the PDZ I-K domain or PDZ L-M domain present in the polypeptides of the instant invention. OBTP (Genbank:NP-037529), for example, is highly expressed in breast cancers and Galectin-3 is highly expressed in pancreatitis, pancreatic cancers, and astrocytic tumors. Muc12 was first isolated as a gene that is down-regulated in colorectal cancer, and BAI3 has been suggested to play a role in suppressing glioblastoma. These tumor-suppressive genes are postulated to exert anti-tumor effects if used in gene therapy. Thus, the isolation of such useful proteins and genes using the instant invention is by itself a very important specific and substantial utility. Such proteins are highly useful as markers for the above-mentioned diseases and can be useful as therapeutic targets for drugs.

Applicants respectfully submit that the foregoing remarks provide uses satisfying the utility guidelines as provided by the "Revised Interim Utility Guidelines Training Materials" published by the U.S. PTO. Accordingly, Applicants respectfully request reconsideration and withdrawal of the §101 rejection.

## **II. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH**

Claims 1-5 and 35-37 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to adequately teach how to use the instant invention. Specifically the Office Action alleges that since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Applicants respectfully traverse this rejection with respect to claim 3 and 35-37.

Applicants respectfully submit that the foregoing comments and the attached §1.132 Declaration establish that the present invention possesses utilities that are specific, substantial, and well-established. Accordingly, Applicants respectfully request withdrawal of the §112, first paragraph rejection.

Claims 1-2 and 4-5 stand rejected under 35 U.S.C. §112, first paragraph because the specification, while being enabling for a substantially pure polypeptide comprising the amino acid sequence as set forth in SEQ ID NO:1 or 2, allegedly does not provide enablement for a polypeptide comprising SEQ ID NO:1 or 2 with up to 50 conservative substitutions or comprising an amino acid sequence of 85% or 90% identity to SEQ ID NO:1 or 2. Applicants respectfully traverse this rejection.

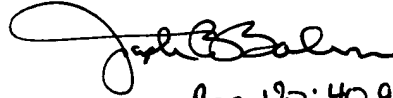
Applicants respectfully submit that modifications and screening of modified polypeptides (e.g., polypeptide having substitutions) of the invention are routine in the art and are set forth by the methods and compositions provided in Applicants' specification. However, in order advance prosecution and/or to provide the claims in better form for appeal, Applicants have canceled claims 1-2 and 4-5, without prejudice. Accordingly, Applicants respectfully request withdrawal of this §112, first paragraph rejection.

Applicant : Shin-Ichi Funahashi et al.  
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Applicants ask that all claims be allowed. Enclosed is a \$110.00 check for the Petition for Extension of Time fee for one (1) month up to and including October 4, 2002. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,



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